UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,917	04/27/2007	Vicki S. Elliott	039386-2277	9780

22428 7590 01/26/2010

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
01/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/554,917	**Applicant(s)** ELLIOTT ET AL.	
	Examiner SHERIDAN SWOPE	**Art Unit** 1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 January 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *3, 4, 6, 7, and 142-144*.
   Claim(s) withdrawn from consideration: *1,2,11,14-20,23,26-32,34,36 and 44-55*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652

Continuation of 11. does NOT place the application in condition for allowance because:

Applicants provide the following arguments to support their request that the rejection under 35 USC 101/112 be withdrawn.
(A) A two-fold difference in expression level is more than sufficient to provide the skilled artisan with a reasonable expectation of successfully distinguishing brain tissue from other tissue types using SEQ ID NO: 56 in a microarray analysis. The specification describes the microarray analysis which illustrates the tissue-specific expression of SEQ ID NO: 56. Therein, a variety of tissue from "at least three different donors" were pooled and used as a reference sample. The expression of SEQ ID NO: 56 was found to be at least 2-fold higher in brain as compared to the reference sample (pg 102, lines 3-12).

(B) Numerous microarray studies have deemed fold-difference values of between 1.4 and 2 fold as significant. See e.g., (1) Yue et al., 2001, reporting a 1.4 fold change in expression as significant (EXHIBIT A), (2) Lee et al., 1999, reporting 1.8 fold induction and 1.6 fold reduction in gene expression as significant (EXHIBIT B); and (3) Vasseur et al., 2003, stating at page 2 that "differential expression values of greater than 1.7 are likely to be significant, based on internal quality control data," however, that a "more stringent ratio" of "at least 2.0 fold" was used (EXHIBIT C).

(C) Reviews on the topic conclude that "there is no magical absolute cut-off for a meaningful fold value" and that essentially, the parameters of each analysis must be considered in determining a meaningful cut-off value for that particular analysis. See e.g., Tsien et al., 2001 (EXHIBIT D).

(D) The Applicants respectfully contend that the Examiner impermissibly raises the utility standard to something which it is not.

These arguments are not found to be persuasive for the following reasons.
(A) Reply: The term "marker" is not defined by the specification. However, the skilled artisan would know that "marker" means something that identifies or that is used to identify a specific trait. Two-fold higher expression of SEQ ID NO: 54 in brain than in the reference sample does not provide evidence that SEQ ID NO: 54 is a specific marker for brain. The reference sample, comprising heart, kidney, lung, placenta, small intestine, spleen, stomarch, testis, and uterus, comprises some tissues having a level of SEQ ID NO: 54 that is higher that the reference sample, which is an average of all included tissues. More likely than not, compared to brain, one or more tissues within the reference sample have the same or higher levels of SEQ ID NO: 54. Therefore, the skilled artisan would not conclude that SEQ ID NO: 54 can be used is a marker to identify brain tissue.

(B) Reply: None of Yue et al, Lee et al, or Vasseur et al discusses using polynucleotides that are tissue-specific markers. Each of said references discusses using a polynucleotide as a probe to detect differences in expression of the complementary polynucleotide in, for example, different tissues (Yue) or due to parameters such as ageing and caloric restriction (Lee), or transformation with ras (Vasseur). In such assays, a 2-fold change may or may not be signigicant, depending on the variability in the compared samples. The skilled artisan would have been aware of statistical methods that can be used to analyze variabilty and determine whether a difference is significant; for example, the Student's t-test. In contrast, for a substance to be considered to be a tissue-specific marker, the expression of the substance in the tissue must be essentially exclusive, i.e., not expressed in other tissues (see (A), above).

(C) Reply: See (A) and (B), above.

(D) Reply: The specification fails to show that the polynucleotide of SEQ ID NO: 54 has a specific, substantial, and credible patentable utility for the reasons explained above and in the prior actions.